

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Venstrom JM, Pittari G, Gooley TA, et al. *HLA-C*-dependent prevention of leukemia relapse by donor activating KIR2DS1. *N Engl J Med* 2012;367:805-16. DOI: 10.1056/NEJMoa1200503

**Supplementary Appendix for NEJM manuscript # 12-00503**

Supplement to: Venstrom JM, et al. *HLA-C-dependent prevention of leukemia relapse by donor activating KIR2DS1.*

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**Supplementary Table 1.** ALL patient and transplant characteristics.

	Donor KIR Genotype	
	KIR2DS1 negative (%)	KIR2DS1 positive (%)
<b>Number of Patients</b>	267 (62.6)	160 (37.5)
<b>Median Age, y (range)</b>	21.51 (0.58-62.48)	21.70 (0.70-54.85)
<b>Disease status<sup>§</sup>, - no. (%)</b>		
High	60 (22.5)	48 (30)
Intermediate	127 (47.6)	65 (40.6)
Low	79 (29.6)	47 (29.4)
Unknown	1 (0.37)	(0)
<b>Year of transplantation - no. (%)</b>		
1988-1994	27 (10.1)	16 (10)
1995-2000	143 (53.6)	82 (51.3)
2001-2006	97 (36.3)	62 (38.8)
<b>HLA matching – no. (%)</b>		
HLA 10 of 10 matched	93 (34.8)	45 (28.1)
HLA 9 of 10 matched	174 (65.2)	115 (71.9)
HLA-A mismatch	42 (24.1)	36 (31.3)
HLA-B mismatch	19 (10.9)	11 (9.6)
HLA-C mismatch	81 (46.6)	42 (36.5)
HLA-DRB1 mismatch	8 (4.6)	11 (9.6)
HLA-DQB1 mismatch	24 (13.8)	15 (13.0)
<b>Transplant type - no. (%)</b>		
Ablative without total-body irradiation	25 (9.4)	12 (7.5)
Ablative with total-body irradiation	233 (87.3)	142 (88.8)
Nonablative or reduced intensity	9 (3.4)	5 (3.1)
Missing	(0)	1 (0.6)
<b>GVHD prophylaxis – no. (%)</b>		
Cyclosporine, methotrexate, +/- other	126 (47.2)	74 (46.3)
Tacrolimus +/- other	47 (17.6)	32 (20)
Other GVHD prophylaxis	4 (0.01)	1 (0.6)
T-cell depletion	90 (33.7)	53 (33.1)
<b>Patient-donor sex - no. (%)</b>		
Female-female	48 (18.0)	30 (18.8)
Female-male	63 (23.6)	38 (23.8)
Male-female	62 (23.2)	29 (18.1)
Male-male	94 (35.2)	63 (39.4)
<b>Patient race- no. (%)</b>		
African American	13 (4.9)	6 (3.8)
Asian/Pacific Islander	6 (2.2)	3 (1.9)
Caucasian	225 (84.2)	132 (82.5)
Hispanic	18 (6.7)	19 (11.9)
Native American	2 (0.7)	(0)
Other/unknown	3 (0.7)	(0)
<b>Source of stem cells - no. (%)</b>		
Bone marrow	229 (85.8)	127 (79.4)
Peripheral blood	38 (14.2)	33 (20.6)
<b>Donor-patient CMV status - no. (%)</b>		
Negative-negative	110 (41.2)	53 (33.1)
Negative-positive	51 (19.1)	34 (21.3)
Positive-negative	63 (23.6)	44 (27.5)
Positive-positive	38 (14.2)	28 (17.5)
Missing	5 (1.9)	1 (0.6)

<sup>§</sup> Low-risk: 1<sup>st</sup> Complete remission; Intermediate: 2<sup>nd</sup> or higher CR; High: primary induction failure or 1<sup>st</sup> or higher relapse

**Supplementary Table 2. Additional KIR and HLA effects on HCT outcome**

Comparison	P-value	Hazard Ratio (95% CI)
<b>Relapse</b>		
Recipient <i>HLA-C1C1</i> * (140/501, 27.9%)		1
Recipient <i>HLA-C1C2</i> (173/568, 30.5%)	0.87	1.02 (0.81-1.28)
Recipient <i>HLA-C2C2</i> (63/164, 38.4%)	0.06	1.34 (0.99-1.82)
Donor <i>KIR2DS1</i> +		
Recipient <i>HLA-C1C1</i> (39/166, 23.5%)		1
Recipient <i>HLA-C1C2</i> (50/193, 25.9%)	0.83	0.95 (0.61-1.49)
Recipient <i>HLA-C2C2</i> (20/53, 37.7%)	0.03	1.92 (1.09-3.39)
Donor <i>KIR2DS1</i> -		
Recipient <i>HLA-C1C1</i> (101/335, 30.1%)		1
Recipient <i>HLA-C1C2</i> (123/375, 32.8%)	0.72	1.05 (0.80-1.38)
Recipient <i>HLA-C2C2</i> (43/11, 38.7%)	0.30	1.21 (0.84-1.75)
Donor <i>KIR2DS1</i> +		
Recipient <i>HLA-C1C1</i> or <i>C1C2</i> (89/351, 25.4%)		1
Recipient <i>HLA-C2C2</i> (20/53, 37.7%)	0.009	1.97 (1.18-3.30)
Donor <i>KIR2DS1</i> -		
Recipient <i>HLA-C1C1</i> or <i>C1C2</i> (224/710, 31.5%)	0.32	1.18 (0.85-1.65)
Recipient <i>HLA-C2C2</i> (43/111, 38.7%)		
<b>Non-Relapse Mortality</b>		
Donor <i>KIR3DS1</i> - (286/811, 35.3%)		1
Donor <i>KIR3DS1</i> + (130/422, 30.8%)	0.13	0.85 (0.69-1.05)
Donor <i>KIR3DS1</i> *		1
Donor <i>KIR3DS1</i> +	0.05	0.74 (0.55-1.00)

\*additionally adjusted for presence of donor *KIR2DS1*

**Supplementary Figure 1.** Specificity of donor *KIR2DS1* and *KIR3DS1* effects on relapse and survival.

